1: J Biol Chem. 1987 Jul 25;262(21):9935-8. Related Article

FREE full text article at www.jbc.org

Platelet glycoprotein IIb-IIIa-like proteins mediate endothelial c attachment to adhesive proteins and the extracellular matrix.

Charo IF, Bekeart LS, Phillips DR.

The adherence of human umbilical vein endothelial (HUVE) cells to adhesiv matrix proteins was examined to determine if cell attachment and spreading mediated by the glycoprotein (GP) IIb-IIIa complex on endothelial cells. The HUVE cells adhered well to glass slides that had been coated with fibronecti vitronectin, fibrinogen, or von Willebrand factor but failed to adhere to albur coated or to uncoated slides. The HUVE cell attachment and spreading on vitronectin, fibrinogen, and von Willebrand factor were greatly inhibited by a IIb-IIIa monoclonal antibody (7E3). In contrast, HUVE cell attachment to fibronectin was not inhibited by 7E3 but was inhibited by a fibronectin-recep antibody (alpha GP140), which had no effect on cell attachment to the other adhesive proteins. The 7E3 antibody, but not alpha GP140, disrupted HUVE monolayers by detaching cells from their naturally occurring extracellular ma These data indicate that platelet GP IIb-IIIa-like proteins mediate the adherer HUVE cells to specific adhesive proteins and to the extracellular matrix.

PMID: 2440865 [PubMed - indexed for MEDLINE]

1: Biochem J. 1993 Jan 15;289 (Pt 2):445-51. Related Article

Evidence for novel binding sites on the platelet glycoprotein IIb IIIa subunits and immobilized fibrinogen.

Parise LV, Steiner B, Nannizzi L, Criss AB, Phillips DR.

Gladstone Institute of Cardiovascular Disease, University of California, San Francisco 94141-9100.

The present study was designed to examine the interaction of the purified pla glycoprotein IIb-IIIa complex (GP IIb-IIIa or integrin alpha IIb beta 3) and th individual subunits of the complex with immobilized fibrinogen. Although 1: GP IIb-IIIa binding to fibrinogen immobilized on Sepharose was specific, thi interaction exhibited properties distinct from those of reversible fibrinogen b: to platelets: 125I-GP IIb-IIIa binding appeared irreversible, but non-covalent (2+)-independent, and was inhibited only weakly, or not at all, by the anti-(G IIIa) monoclonal antibodies 10E5 and 7E3 and synthetic peptides from know platelet-binding domains of fibrinogen. Reversibly dissociated GP IIb or GP subunits inhibited 125I-GP IIb-IIIa binding to immobilized fibrinogen and bc directly to the fibrinogen. However, these subunits did not bind to peptides d from known platelet-binding domains within the fibrinogen alpha- and gamn chains, although the GP IIb-IIIa complex did. These results show that the complexed form of full-length GP IIb and GP IIIa is required for binding to t synthetic peptides, but not necessarily for binding to immobilized fibrinogen GP IIb-IIIa can bind to immobilized fibrinogen by a distinct mechanism that appears to involve novel binding sites on each subunit of the GP IIb-IIIa com and on fibrinogen.

PMID: 8424789 [PubMed - indexed for MEDLINE]

ANTICANCER DRUGS 1996 7:723-7

1: Br J Cancer. 1998 Mar;77(6):956-64. Related Article

Comment in:
- Br J Cancer. 1999 Jan;79(2):370-3.

Release of the angiogenic cytokine vascular endothelial growth f (VEGF) from platelets: significance for VEGF measurements ar cancer biology.

Banks RE, Forbes MA, Kinsey SE, Stanley A, Ingham E, Walters C, Sell

ICRF Cancer Medicine Research Unit, St James's University Hospital, Leeds

Vascular endothelial growth factor (VEGF) is a potent angiogenic factor witl key role in several pathological processes, including tumour vascularization. preliminary observations indicated higher VEGF concentrations in serum sar than in matched plasma samples. We have now demonstrated that this differe due to the presence of VEGF within platelets and its release upon their activa during coagulation. In eight healthy volunteers, serum VEGF concentrations ranged from 76 to 854 pg ml(-1) and were significantly higher ($P < 0.01$) tha matched citrated plasma VEGF concentrations, which ranged from < 9 to 42 (-1). Using platelet-rich plasma, mean (s.d.) platelet VEGF contents of 0.56 (pg of VEGF 10(-6) platelets were found. Immunocytochemistry demonstrate cytoplasmic presence of VEGF within megakaryocytes and other cell types v the bone marrow. From examination of the effects of blood sample processin circulating VEGF concentrations, it is apparent that for accurate measuremer citrated plasma processed within 1 h of venepuncture should be used. Serum completely unsuitable. The presence of VEGF within platelets has implicatio processes involving platelet and endothelial cell interactions. e.g. wound hea and in tumour metastasis, when platelets adhering to circulating tumour cells release VEGF at points of adhesion to endothelium, leading to hyperpermeat and extravasation of cells.

PMID: 9528841 [PubMed - indexed for MEDLINE]

* PNAS 1/1997 94:663-8

CLIN CANCER RES 12/1997 3:2187-90

EUR J CANCER 1996 32A 2401-12

1: Clin Cancer Res. 1997 Dec;3(12 Pt 1):2187-90. Related Article

Platelet: transporter of vascular endothelial growth factor.

Verheul HM, Hoekman K, Luykx-de Bakker S, Eekman CA, Folman C(Broxterman HJ, Pinedo HM.

Department of Medical Oncology, University Hospital "Vrije Universiteit,"] MB Amsterdam, The Netherlands.

In animal models, growth of tumors and their metastases is dependent on fac that stimulate vessel formation (angiogenesis). Most clinical studies confirm importance of angiogenesis for cancer growth in patients. Recent studies on circulating angiogenic factors in patients have focused on serum vascular endothelial growth factor (VEGF) levels in a variety of cancer types. We me: serum VEGF concentrations and blood counts in 27 breast cancer patients du each of 6 cycles of chemotherapy with doxorubicin and cyclophosphamide supported by granulocyte macrophage colony-stimulating factor. Serum VE(concentrations highly correlated with platelet counts during chemotherapy (r $P < 0.01$). In particular, during the first treatment cycle, after an initial episoc thrombocytopenia, a strong platelet rebound coincided closely with a serum peak ($r = 0.9$; $P < 0.01$). In addition, plasma VEGF concentrations from 15 o cancer patients and 30 healthy volunteers were 5- to 8-fold lower than their corresponding serum VEGF concentrations ($P < 0.001$). Activation of platele increased the VEGF content 8-10 times. These findings demonstrate that VE released by platelets during serum preparation. In this study, we found evide VEGF transport by platelets, indicating that serum VEGF concentrations refl mainly platelet counts rather than tumor burden in cancer patients, as reporte earlier. Platelets, known to be important for wound healing, have also been reported to contribute to metastasis formation and tumor growth in animal m Indeed, tumors can be regarded as never-healing wounds. Our data suggest tl platelets may have a stimulating role on angiogenesis-dependent tumor grow through their function as transporters of VEGF.

PMID: 9815613 [PubMed - indexed for MEDLINE]

LANCET 1996 352:1775

ANGIOGENESIS + Lm609 + VITRONECTIN

INT J CANCER 1997 71:320-4

J CLIN INVEST 96:1815-22 1995